

From the INTERNATIONAL BUREAU

**PCT****NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C.20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

01 August 2000 (01.08.00)

International application No.

PCT/US99/27191

Applicant's or agent's file reference

UMARY 5 WO

International filing date (day/month/year)

17 November 1999 (17.11.99)

Priority date (day/month/year)

17 November 1998 (17.11.98)

Applicant

DEMIREV, Plamen, A. et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

19 June 2000 (19.06.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Antonia Muller

Telephone No.: (41-22) 338.83.38



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p><b>(51) International Patent Classification <sup>6</sup> :</b> <b>G06F 17/30</b></p>	<b>A1</b>	<p><b>(11) International Publication Number:</b> <b>WO 00/29987</b></p> <p><b>(43) International Publication Date:</b> 25 May 2000 (25.05.00)</p>																		
<p><b>(21) International Application Number:</b> PCT/US99/27191</p> <p><b>(22) International Filing Date:</b> 17 November 1999 (17.11.99)</p> <p><b>(30) Priority Data:</b></p> <table style="width: 100%;"> <tr> <td style="width: 30%;">60/108,696</td> <td style="width: 40%;">17 November 1998 (17.11.98)</td> <td style="width: 30%;">US</td> </tr> <tr> <td>60/120,679</td> <td>19 February 1999 (19.02.99)</td> <td>US</td> </tr> </table> <p><b>(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications</b></p> <table style="width: 100%;"> <tr> <td style="width: 30%;">US</td> <td style="width: 40%;">60/108,696 (CIP)</td> <td style="width: 30%;"></td> </tr> <tr> <td>Filed on</td> <td>17 November 1998 (17.11.98)</td> <td></td> </tr> <tr> <td>US</td> <td>60/120,679 (CIP)</td> <td></td> </tr> <tr> <td>Filed on</td> <td>19 February 1999 (19.02.99)</td> <td></td> </tr> </table> <p><b>(71) Applicant (for all designated States except US):</b> UNIVERSITY OF MARYLAND [US/US]; Office of Technology Liaison, 4312 Knox Road, College Park, MD 20742 (US).</p> <p><b>(72) Inventors; and</b></p> <p><b>(75) Inventors/Applicants (for US only):</b> DEMIREV, Plamen, A. [BG/US]; Dept. of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742 (US). FENSELEAU, Catherine [US/US]; Dept. of Chemistry and Biochemistry, University of Maryland, College Park, MD 20742 (US).</p>		60/108,696	17 November 1998 (17.11.98)	US	60/120,679	19 February 1999 (19.02.99)	US	US	60/108,696 (CIP)		Filed on	17 November 1998 (17.11.98)		US	60/120,679 (CIP)		Filed on	19 February 1999 (19.02.99)		<p><b>(74) Agents:</b> LEBOVITZ, Richard, M. et al.; Millen, White, Zelano &amp; Branigan, P.C., Arlington Courthouse Plaza 1, Suite 1400, 2200 Clarendon Boulevard, Arlington, VA 22201 (US).</p> <p><b>(81) Designated States:</b> AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report.</i></p>
60/108,696	17 November 1998 (17.11.98)	US																		
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US	60/120,679 (CIP)																			
Filed on	19 February 1999 (19.02.99)																			
<p><b>(54) Title:</b> METHODS FOR IDENTIFYING AND CLASSIFYING ORGANISMS BY MASS SPECTROMETRY AND DATABASE SEARCHING</p> <p><b>(57) Abstract</b></p> <p>A method for rapid identification of biological materials is presented, which exploits the wealth of information contained in genome and protein sequence databases (5). In a preferred embodiment, the method utilizes the masses of a set of ions by MALDI TOF mass spectrometry of intact or treated cells (1). Subsequent correlation (4) of each ion in the set to a protein, along with the organismic source of the protein, is performed by searching a database comprising protein molecular weights (9).</p>																				
<p style="text-align: center;"><b>AN EXAMPLE OF A SOFTWARE FLOW CHART FOR MICROORGANISM AND CELL IDENTIFICATION BY MASS SPECTROMETRY AND DATA BASE SEARCH</b></p> <pre> graph TD     1[Input masses from mass spectrum. 1] --&gt; 2[Process masses: Deconvolute multiply-charged ion series, subtract z (no. protons x 1 Da), convert to average (or monoisotopic) mass, etc. 2]     2 --&gt; 3[Set mass window. 3]     3 --&gt; 4[Search protein database for mass matches. 4]     5[Optional inputs: specify mass range, organism type, database, etc. 5] --&gt; 4     4 --&gt; 6[List all proteins in each window, their masses and organismic sources. 6]     6 --&gt; 7[Refine and reduce number of possible proteins in each window. 7]     8[Input proteolytic peptide masses, sequence tags from MS/MS spectra, other information. 8] --&gt; 7     7 --&gt; 9[Score and rank organismic sources based on: number of proteins identified, total number of proteins, and other criteria, additional information. 9]     9 --&gt; 10[Iterate e.g. correct masses for possible metal ion adducts, post-translational modifications (methylation, acetylation, methionine loss, etc.) 10]     10 --&gt; 2     7 --&gt; 6     9 --&gt; 11[Output list of identified source organisms. 11]   </pre>																				

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
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## PATENT COOPERATION TREATY

## PCT

REC'D 22 JAN 2001

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UMARY 5 WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/27191	International filing date (day/month/year) 17 NOVEMBER 1999	Priority date (day/month/year) 17 NOVEMBER 1998
International Patent Classification (IPC) or national classification and IPC IPC(7): G06F 17/30 and US Cl.: 707/6.102.104		
Applicant UNIVERSITY OF MARYLAND		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

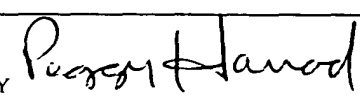
2. This REPORT consists of a total of 4 sheets.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 19 JUNE 2000	Date of completion of this report 04 JANUARY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer WAYNE AMSBURY 
Facsimile No. (703) 305-3230	Telephone No. (703) 305-3900

**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☐ the international application as originally filed
- ☒ the description:  
pages \_\_\_\_\_ (See Attached) \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

- ☒ the claims:  
pages \_\_\_\_\_ (See Attached) \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, as amended (together with any statement) under Article 19  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

- ☒ the drawings:  
pages \_\_\_\_\_ (See Attached) \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

- ☒ the sequence listing part of the description:  
pages \_\_\_\_\_ (See Attached) \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

**4. ☒ The amendments have resulted in the cancellation of:**

- ☒ the description, pages \_\_\_\_\_ NONE \_\_\_\_\_
- ☒ the claims, Nos. \_\_\_\_\_ NONE \_\_\_\_\_
- ☒ the drawings, sheets/fig \_\_\_\_\_ NONE \_\_\_\_\_

**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments. (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/27191

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. statement

Novelty (N)	Claims	<u>1-11</u>	YES
	Claims	<u>NONE</u>	NO
Inventive Step (IS)	Claims	<u>1-11</u>	YES
	Claims	<u>NONE</u>	NO
Industrial Applicability (IA)	Claims	<u>1-11</u>	YES
	Claims	<u>NONE</u>	NO

## 2. citations and explanations (Rule 70.7)

Claims 1-10 MEET the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the use of intact, undigested proteins within the context of the claims.

----- NEW CITATIONS -----  
NONE

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**I. BASIS OF REPORT:**

This report has been drawn on the basis of the description,  
page(s) 1-28, as originally filed.  
page(s) NONE, filed with the demand.  
and additional amendments:

This report has been drawn on the basis of the claims,  
page(s) NONE, as originally filed.  
page(s) NONE, as amended under Article 19.  
page(s) NONE, filed with the demand.  
and additional amendments:  
Pages 29-30, filed with the letter of 24 October 2000.

This report has been drawn on the basis of the drawings,  
page(s) 1-8, as originally filed.  
page(s) NONE, filed with the demand.  
and additional amendments:  
NONE

This report has been drawn on the basis of the sequence listing part of the description:  
page(s) NONE, as originally filed.  
pages(s) NONE, filed with the demand.  
and additional amendments:  
NONE

PCT/US 99/27191

IPEA/US 42 OCT 2000  
24

**Claims:**

1. A method of identifying one or more unknown microorganisms in a sample, comprising:

5 searching a sequence database for a plurality of intact, undigested proteins that are predicted to have the molecular weights of proteins in a mass spectrum of a sample, whereby said one or more unknown microorganisms are identified,

wherein said sample comprises a plurality of intact, undigested proteins from one or more unknown microorganisms, and said database is searched for more than one different protein.

10 2. A method of claim 1, wherein the sequence database is a protein sequence database.

3. A method of claim 1, wherein the sequence database is a nucleotide sequence database.

15 4. A method of claim 1, wherein the mass spectrometry data is MALDI-TOF data.

5. A method of claim 1, wherein the mass spectrometry data is obtained by electrospray on a time-of-flight, quadrupole, or ion trap mass analyzer.

20 6. A method of claim 1, further comprising:  
performing a mass spectral analysis on a sample comprising one or more microorganisms.

7. A method of claim 1, further comprising:  
identifying molecular weights of proteins in a mass spectrum of said sample.

**ENDED SHEET**



8. A method of claim 1, wherein said sample comprises at least two different species of microorganisms.

9. A method of claim 1, wherein the sequence database is the NCBI/SwissProt/EMBL database.

5 10. A method of claim 1, further comprising chemical or enzymatic digestion of a protein in said sample.

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: RICHARD M. LEOVITZ  
MILLEN, WHITE, ZELAND & BRANIGAN, P.C.  
ARLINGTON COURTHOUSE PLAZA I  
2200 CLARENDON BOULEVARD, SUITE 1400  
ARLINGTON, VA 22201

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing (day/month/year)	<b>09 FEB 2000</b>
Applicant's or agent's file reference  UMARY 5 WO	FOR FURTHER ACTION    See paragraphs 1 and 4 below
International application No.  PCT/US99/27191	International filing date (day/month/year)  17 NOVEMBER 1999
Applicant  UNIVERSITY OF MARYLAND	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

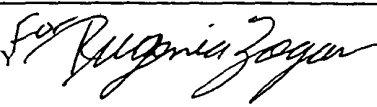
- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  Facsimile No. (703) 305-3230	Authorized officer WAYNE AMSBURY   Telephone No. (703) 305-3900
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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UMARY 5 WO	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US99/27191	International filing date (day/month/year) 17 NOVEMBER 1999	(Earliest) Priority Date (day/month/year) 17 NOVEMBER 1998
Applicant UNIVERSITY OF MARYLAND		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (See Box I).
2. ☐ Unity of invention is lacking (See Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - ☐ filed with the international application.
  - ☐ furnished by the applicant separately from the international application,
    - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - ☐ transcribed by this Authority.
4. With regard to the title,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - ☐ the text is approved as submitted by the applicant.
  - ☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:  
Figure No. 6
  - ☐ as suggested by the applicant.
  - ☒ because the applicant failed to suggest a figure.
  - ☐ because this figure better characterizes the invention.☐ None of the figures.

## Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

A method for rapid identification of biological materials is presented, which exploits the wealth of information contained in genome and protein sequence databases (5). In a preferred embodiment, the method utilizes the masses of a set of ions by MALDI TOF mass spectrometry of intact or treated cells (1). Subsequent correlation (4) of each ion in the set to a protein, along with the organismic source of the protein, is performed by searching a database comprising protein molecular weights(9).

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/27191

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : G06F 17/30

US CL : 707/6,102,104

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 707/6,102,104

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,538,897 A [YATES,III ET AL] 23 JUNE 1996, COL3 1-2	1-11 —
Y	US 5,809,212 A [SHASHA] 15 SEPTEMBER 1998, COLS 1-5	1-11 —
Y,P	US 5,869,240 A [PATTERSON] 09 FEBRUARY 1999, COLS1-4	1-11 —
Y,P	US 5,930,803 A [BECKER ET AL] 27 JULY 1999, COLS 1-5	1-11 —
Y,P	US 5,930,784 A [HENDRICKSON] 27 JULY 1999, COLS 1-2	1-11 —
Y,P	US 5,977,890 A [RIGOUTSOS ET AL] 02 NOVEMBER 1999	1-11 —

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*B* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

31 JANUARY 2000

Date of mailing of the international search report

09 FEB 2000

 Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231  
 Facsimile No. (703) 305-3230

Authorized officer

WAYNE AMSBURY

Telephone No. (703) 305-3980

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US99/27191

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,986,652 A [MEDL ET AL] 16 NOVEMBER 1999, COLS 1-4	1-11 —
Y,P	US 5,987,470 A [MEYERS ET AL] 16 NOVEMBER 1999, COLS 1-2	1-11 —